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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/500,512	02/09/2000	Richard A. E. Clark	001.00251	6713

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EXAMINER	
KIM, VICKIE Y	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/500,512	CLARK ET AL.	
	Examiner	Art Unit	
	Vickie Kim	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *26-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments, see paper No.10, filed Jan. 18, 2002, with respect to the rejection(s)of claim(s) 1-25 and 33-34 under 103 for obviousness over US patent 5,935,850 (Clark et al) in view of Brown et al(1993) and Mosesson et al(1966), have been fully considered and applicant's argument is considered to be persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Greiling et al (1997) in view of DeMoraes(1998, Rev Paul Med).

Status of Application

2. Claims 1-34 are pending.

3. The elected claims 1-25 and 33-34 are presented for the examination.

4. The non-elected claims 26-32 are withdrawn from consideration.

Claim Rejections - 35 USC §102/103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-25 and 33-34 are rejected under 35 U.S.C. as anticipated by DeMoraes et al (1998, Rev Paul Med) or, in the alternative, under 35 U.S.C. 103(a) as obvious

over DeMoraes et al (1998, Rev Paul Med) in view of Greiling et al(1997, Fibronectin..) and Mossessen.

Claims are drawn to a method of enhancing fibroblast migration by contacting the wound site with fibrinogen processed by precipitating plasma with glycine.

DeMoraes et al teach a use of fibrin glue into the wound site in dermatologic surgery where substantial tissue injury is occurred to enhance the wound healing via stimulating the formation of granulation tissue, see abstract. Demoraes et al also teach that plasma containing fibrinogen produces the fibrin glue by contacting with thrombin via centrifugation, precipitation(e.g cryoprecipitation) techniques and purified via the glycine precipitation technique, see pages 1748-1749. Although applicant's claims differ because they require fibroblast migration, one would have envisaged the enhanced migration of fibroblast to form granulation tissue in the wound site because same plasmatic fibrinogen precipitated with glycine is taught in both cited reference and the instant claims and fibroblast migration to fibrin(fibrinogen) is already conventional knowledge to the skilled artisan wherein the exogenous fibrinogen is responsible for the enhancement of fibroblast migration in addition to the endogenous fibrinogen produced in injured tissues as evidenced by numerous documents and applicant's own admission in the instant specification (see pages 4-5 of the instant specification and PTO-892 for supporting document).

Thus, it is inherent feature that is naturally occurring when the fibrin glue of DeMoraes et al is applied to the wound site and the claimed subject matter is already

achieved by Demoraes's wound treatment that utilizes fibrinogen contained in fibrin glue into the wound.

Even if, this examiner's allegation is not fully persuasive, the claimed subject matter is not patentably distinct over the prior art of the record when De Moraes et al is taken in view of Greiling et al because Greiling et al(1997) teach a fibroblast migration to fibrin clot in the wound area after substantial tissue injury, wherein said fibroblast transmigrates to fibrin clot and contribute to the formation of granulation tissue and eventually enhances the wound healing process, see abstract. The fibroblast transmigration is in the wound area after substantial tissue injury into the fibrin which contains fibrinogen as a main ingredient, see page 863. Greiling et al further teach that cytokines, PDGF(platelet-derived growth factor BB), platelet releasate, fibronectin are beneficially included in said fibrin gel to increase the fibroblast migration so the wound repair and healing can be potentiated, see abstract and page 862, 3rd paragraphs.

Although De Moraes et al does not explicitly explain the underlying mechanism, said underlying mechanism wherein the wound healing via granulation tissue formation is achieved by fibroblast migration into fibrin(wound site), is already well acknowledged by any ordinary skilled artisan at the time of the invention was made as well as the teaching of Greiling et al and also evidenced by numerous documents(see PTO-892). Therefore, One would have been motivated to apply fibrin glue that contains plasmatic fibronogen purified with glycine to enhance the fibroblast migration so the maximum therapeutic effects can be achieved in addition to the endogenous fibrin clot formed in wound site. One would have been motivated to add extra beneficial additives such as

cytokines, PDGF(platelet-derived growth factor BB), platelet releasate, fibronectin are beneficially included in said fibrin gel to increase the fibroblast migration so that the wound repair and healing can be potentiated. It is noted that said additives are lipids which is well recognized in the art, see evidentiary documents(PTO-892). One would have been motivated to make highly purified fibronogen containing fibrin glue(gel) to increase the therapeutic efficacy because the contamination may cause unwanted result (e.g. plasminogen that causes unwanted fibrinolysis) or decreased fibroblast migration.

As to the claims 2-25 and 33-34 are included in this rejection because the procedure required for purification and precipitation is taught by both cited references, and the minor differences do not render the claims patentably distinct over the teaching of each reference. For instance, De Moraes et al teach centrifugation, separation of plasma from supernatants(required by the instant claims 5, 9-10,12-17), and the pH=7.4 of final product(required by the instant claim 6) and a final concentration of glycine about 2.2M/l(required by the instant claims 8, 11),see page 1749.

As mentioned in previous office action, Mosessen teaches Mosesson et al teach a method for the preparation of highly purified human fibrinogen having a clottability of about 98% via repeated precipitation of plasma with glycine(starting materials). For instance, temperature (i.e. 2-5°) , the concentration of glycine(e.g. 2.1M), the pH of solution(e.g. about 7-8), see pages 2830-2832. Mosesson et al teach reprecipitation with glycine to increase clottability more than 97% and conditions required for

processing such precipitation. For instance, the reprecipitation in a buffer, the addition of ammonium sulfate, lipid-proteins, see pages 2833-2834.

Since Demoraes et al's precipitation is same method of Mosessen's wherein both method is related to the purification of plasma fibrinogen utilizing glycine precipitation method, all the claimed subject matter is not patentably distinct over the prior art and the limitations recited in the dependent claims are properly included in this rejection because all the steps required for the process of purification and precipitation is inherently same and possessed by DeMoraes et al's treatment, or alternatively, obvious over the prior art of the record.

Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product by process claim is the same as or obvious from a product of the prior art, the claim is unpatentably even though the prior product was made by a different process, *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966(Fed. Cir. 1985). In this case, fibrin gel containing fibrinogen precipitated and purified with glycine and buffer, the product used in the claims are same as one taught by the cited reference. Especially, fibrinogen is responsible for the fibroblast migration, and thus, one would have expect the reasonable success from fibrinogen containing fibrin gel taught by each cited reference.

The structure implied by the process steps should be considered when assessing the patentability of product –by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or

where the manufacturing process steps would by expected to impart distinctive structural characteristics to the final product, See e.g., *In re Garnero*, 412 F. 2d 276, 279, 162 USPQ 221, 223 (CCPA 1979).

The minor variations including the selection of optimal environment and steps in order to determine the most effective treatment is well within the skilled level of artisan having ordinary skill in the art, and is obvious.

Conclusion

7. No claim is allowed.

8. This is 3rd Non-final rejection.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 703-305-1675. The examiner can normally be reached on Tuesday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 703-308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-3165 for regular communications and 703-746-3165 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

VICKIE KIM
PRIMARY EXAMINER

Vickie Kim,
Patent examiner
May 15, 2004
Art unit 1614